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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,195	12/03/2003	Shan Lu	17738-003001 / UMMC 03-24	7308

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,195	LU ET AL.	
	Examiner	Art Unit	
	Bo Peng	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-60 and 81-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-60 and 81-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~1/14/08~~ 3-2-05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction election

1. The Office acknowledges the receipt of Applicant's restriction election filed on September 22, 2005. Applicant elects the invention of Group IV, claims 53-60, without traverse.

2. The Office also acknowledges Applicant's Amendment filed on October 4, 2005. Claims 1-52 and 61-80 have been canceled. Claims 53, 54 and 58-60 have been amended. Claims 81-110 have been added. Accordingly, claims 53-60 and 81-110 are pending. Claims 53-60 and 81-110 are examined in the instant Office action.

Information Disclosure Statement

3. The information disclosure statement submitted on March 2, 2005 is in compliance with the provisions of 37 CRF 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

4. An initialed and dated copy of Applicant's IDS form 1449 is attached to the instant Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 54-60, and 81-93, 95-106, and 108-110 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. Claims 54-60, and 81-93, 95-106, and 108-110 recite a method of inducing immune responses against HIV. The method comprises administering to a mammal a nucleic acid composition comprising a plurality of sets of nucleic acid molecules which encode an HIV envelope glycoprotein of a type or a genetic clade, and further administering to the mammal a protein composition comprising a set of isolated HIV envelope proteins. Since the limitation of "a nucleic acid composition" is nucleic acid molecules that encodes an HIV envelope protein of a type or genetic clade, and the limitation of "a protein composition" is HIV envelope glycoproteins, the scope of "a nucleic acid composition" and "a protein composition" encompasses any HIV envelope genes or proteins, including those of any known, unknown, wild type, primary, laboratory-adapted, and recombinant strains of HIV-1 and HIV-2. Although the claims read on the nucleic acid and protein compositions with no limitation, the specification does not reasonably convey possession of all HIV envelope genes and proteins. In the specification, Applicant has disclosed a few species of envelope genes and proteins of HIV-1 clades A, B, C, D, E, F and G, but has not disclosed sufficient species of vaccines support the broadly claimed genus of envelope DNA or proteins of all HIV.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detail chemical structure of the encompassed genus of undefined nucleotide fragment, proteins or polypeptides. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Lid.*, 18 USPQ2d 1016.

7. Consequently, while the skilled artisan would reasonably conclude Applicant was in possession of envelope genes and proteins of a few HIV-1 strains, such as those of one or two strains of each clade A, B, C, D, E, F and G, there is no indication that Applicant was in possession of all envelope genes and proteins of HIV-1 clades A, B, C, D, E, F and G; neither those of clades H, I, J or K, nor those of O and N group of clades, nor those of non-classified, and nor those of an entire HIV genus as broadly claimed.

8. Claim 53 is further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

9. Claim 53 is broadly directed toward a method of treating an individual with AIDS, the method comprising administering to the individual a protein composition comprising a plurality of sets of HIV envelope proteins of a genetic clade in amount sufficient to inhibit disease progression due to HIV.

10. The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

11. A person of skill in the art is not enabled to make and use the method of treating an individual with AIDS with the scope of the claims as presently recited, because there is insufficient disclosure to enable the claimed invention. It is well known in the art that

development of therapeutic HIV vaccine remains a challenge (Vandepapeliere 2002). Common problems encountered with treating HIV infection include the extraordinary variability, or quasispecies nature, of HIV, the existence of a latent form of the virus, and dysfunctions of the host immune system. The plasticity of the HIV-1 genome and its contribution to immune escape are salient factors that have prevented the development of protective immunity in HIV infected patient. Even when a neutralizing antibody or CD8+ response is generated after immunization, it rapidly becomes ineffective as other members of the quasispecies quickly replicate and grow out. To date, several clinical trials have been conducted but in every situation, the immunogen failed to induce protective immunity, failed to control viremia, and failed to protect individuals at a high risk from infection. The potential application of HIV envelope protein as a therapeutic vaccine against chronic HIV infection has been studied with "Vaxsyn", a recombinant HIV envelope subunit gp160 vaccine (Pontesilli 1998). Although early phase I studies showed VaxSyn to be immunogenic and safe, Vaxsyn has failed to show any efficacy in HIV-1 infected individuals in Phase II trial.

12. The state of the prior art has shown that development of a therapeutic vaccine against HIV infection is unpredictable. The less is known about the art of the invention in the prior art, the more details would need in the specification as to how to use the invention in order for a person of skill in the art to be enabled to use the claimed invention. The disclosure, however, fails to provide any working embodiments to show that claimed HIV envelope proteins are capable of overcoming the obstacles discussed above and conferring protection. It is not clear what type of immune response is induced to provide a therapeutic benefit by the claimed HIV envelope proteins, which can suppress quansispecies of HIV, clear up HIV-infected cells,

resulting in the "inhibition of disease progress". Even though the skill in the art is high, given the lack of guidance and working examples, the quantity of experimentation necessary to practice the claimed invention is undue. Therefore, considering the broad scope of the claim, the complex state and nature of the art, unpredictability from the prior art, Applicant has not provided sufficient information to enable the full breath of the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 54-60, 81-90, 93, 97, 109 and 110 are rejected under 35 U.S.C. 102(a) as being anticipated by Barnett (1997).

14. Claims 54-60, 81-90, 93, 97 109 and 110 are directed to a method of inducing an immune responses against HIV, the method comprising administering to a mammal a nucleic acid composition comprising a plurality of sets of nucleic acid molecules encode an HIV envelope glycoprotein of a type or a genetic clade, and further administering to the mammal a protein composition comprising a set of isolated HIV envelope proteins.

15. Using BALB/c mice and Guinea pig as animal models, Barnett teaches a method of inducing immune responses using priming immunization with a DNA plasmid vaccine containing envelope genes of primary strains, HIV-1_{US4} (clade B) and HIV-1_{CM235} (clade E), and boosted with their proteins. Both humoral and cell-mediated immune responses were tested. Barnett teaches that the DNA prime/subunit protein boost may be safe and less costly alternative vaccination strategy because the ability of HIV DNA vaccines to effectively and reproducibly induce immune responses.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 54 and 96 rejected under 35 U.S.C. 103(a) as being unpatentable over Andre (1998).

17. Claims 54 and 96 are directed to a method of inducing immune responses in a mammal by DNA prime/protein boosting immunization, wherein one of more of DNA vaccines comprises optimized codons.

18. Andre teaches an HIV gp120 DNA vaccine whose gene codons are optimized for improved expression in human cells. Andre teaches that the DNA vaccine containing optimized

condon usage considerably increases the gene expression in human cells, resulting enhanced immune responses in BALB/c mice.

19. It is recognized in the art of the DNA vaccine development that codon optimization of viral antigen in DNA vaccines is an effective approach to increase the immunogenicity of the DNA vaccine. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to optimize the codon of the claimed HIV envelope genes with the expectation of success, so that to increase its immunegencity. Therefore, the invention as a whole was *prima facie* obvious over Andre.

20 Claims 54, in part, 91, 92, 94, 95, 97-108 are rejected under 35 U.S.C. 103(a) as being obviousness over Barnett (1997) and Gao (1996).

21. Claims 54, in part, and 98-106 are directed to a method of inducing immune responses in a mammal comprising immunizing the mammal with multiple sets of HIV envelope DNAs and multiple HIV envelope proteins of different clades.

22. The relevance of Barnett is given above.

23. Gao teaches a panel of envelope genes from HIV-1 clade A to G. Gao also suggests that the panel of envelope genes from HIV-1 clade A to G should prove valuable for AIDS vaccine development efforts targeted against a broader spectrum of viruses.

> MPEP § 2144.06 recites the conclusions of *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA), "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art."

> The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker. 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). See MPEP 2144.

24. The claims are drawn to both HIV envelope genes and proteins as a vaccine composition to induce immune responses in a mammal. HIV envelope proteins have been the objects of intensive research in the prior art as a vaccine candidate. The envelope genes and proteins of primary isolates used in the instant invention are known and their application for AIDS vaccine development is suggested in the prior art (Gao 1994 and 1996). Since the instant invention is drawn to combining some envelope genes and proteins of known HIV isolates to induce immune responses in a mammal, the combination of their additive effects renders the invention prima facie obvious and does not exhibit an unexpected result.

25. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine envelope of different clades to increase the breadth of reactivity across genetic clades. One skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Therefore, the invention as a whole was *prima facie* obvious over Barnett and Gao.

Remarks

26. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D., whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

JEFFREY STUCKER
PRIMARY EXAMINER

Bo Peng, Ph.D.
11/07/05